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RAPID HEALTH TECHNOLOGY ASSESSMENT:

Hypoglossal nerve stimulation for the treatment of obstructive sleep apnoeas

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Innhold

Key messages

Obstructive sleep apnea (OSA) is a sleep disorder characterized by frequent interruption in breathing (apnoea) due to the narrowing or closure of the soft pharyngeal tissue while asleep. This is a risk factor for cardiovascular, neurological, and metabolic conditions. Current clinical practice involves treatment with continuous positive airway pressure (CPAP) during sleep. Many patients have a low tolerance for CPAP treatment, and the compliance rate can be as low as 50%. Hypoglossal nerve stimulation (HNS) is a possible alternative for patients who do not tolerate CPAP. The method, which is illustrated in this rapid HTA, keeps the airways open by stimulating the hypoglossal nerve during sleep.

Effect and safety: An HTA published by EUnetHTA in June 2020 included one randomized controlled trial (n = 46) and seven uncontrolled studies. The effect of hypoglossal nerve stimulation in the treatment of obstructive sleep apnea is generally very uncertain. Several relevant studies are expected to publish results in 2022 and 2023.

Severity: Severity is not calculated as this rapid HTA does not include a health economic assessment of cost-effectiveness.

Costs: The equipment costs are estimated at NOK 270,000 per patient. The clinical experts estimate that the first year will be 100 relevant patients but expect the use to increase with 25-30 percent each year. In such a scenario, the total annual costs for equipment will be estimated at NOK 27 million in the first year and NOK 72 million in year five. This estimate does not include cost related to the surgical procedures.

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Hypoglossal nerve stimulation for the treatment of obstructive sleep apnoea: a rapid HTA

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Hovedbudskap

Obstruktiv søvnapne (OSA) er en søvnforstyrrelse karakterisert ved hyppige pusteforstyrrelser under søvn fordi faryngalt vev kollapser. Dette utgjør en risikofaktor for kardiovaskulære, nevrologiske og metabolske tilstander. Gjeldende klinisk praksis innebærer behandling med kontinuerlig positive luftveistrykk (CPAP) gjennom en mask under søvn. Mange pasienter har lav toleranse for behandling med CPAP, og etterlevelsesandelen kan være så lav som 50%. Hypoglossal nervestimulering (HNS) er et mulig alternativ til pasienter som ikke tolererer CPAP. Metoden, som belyses i denne forenklede metodevurderingen, holder luftveiene åpne ved å stimulere den hypoglossale nerven under søvn.

Effekt og sikkerhet: En metodevurdering utgitt av EUnetHTA i juni 2020 omfattet èn randomisert kontrollert studie (n=46) og sju ukontrollerte studier. Effekten av hypoglossal nervestimulering i behandling av obstruktivt søvnapné er gjennomgående svært usikker. Det pågår flere relevante studier som forventes å publisere resultater i 2022 og 2023.

Alvorlighet: Alvorlighetsgrad er ikke beregnet ettersom dette er en forenklet metodevurdering uten helseøkonomisk vurdering av kostnadseffektivitet.

Kostnader: Prisen for utstyret estimeres til NOK 270 000 per pasient. Fagekspertene anslår at det første år vil være 100 aktuelle pasienter, men regner med en årlig økning på 25-30 prosent. De totale årlige kostnadene for utstyr vil i et slikt scenario estimeres til 27 MNOK første år og 72 MNOK i år fem. Denne kostnaden omfatter ikke kirurgiske kostnader som er nødvendig for å operere inn utstyret.

Tittel:
Hypoglossal nervestimulering for behandling av obstruktiv søvnapné: en forenklet metodevurdering

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Hvem står bak denne publikasjonen?
Folkehelseinstituttet

Når ble litteratursøket avsluttet?
Januar 2020

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Preface

Division for health services in Norwegian institute of public health (NIPH), received a commission from The National System for Managed Introduction of New Health Technologies in Norway. In the commission, NIPH was asked to deliver a rapid health technology assessment about nerve stimulation in the treatment of obstructive sleep apnoea.

Division for health services in NIPH follows a common procedure when working with systematic reviews and health technology assessment. This rapid HTA is based on a health technology assessment published by EUnetHTA in June 2020.

Bidragsytere
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We tank Håkon Pharo Skaug at Vestre Viken HF and Britt Kari Stene at St. Olavs hospital HF for valuable contributions in the project.

Conflict of interest
All authors and experts have filled out a form that identifies possible conflicts of interest. No one states conflicts of interest.

NIPH is responsible for the content in this report.

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Background

Obstructive sleep apnoea (OSA)

Obstructive sleep apnoea (OSA) occurs in 1 out of 6 persons in Norway and its prevalence ranges between 8 and 16%, depending on severity (1, 2). OSA is a condition characterized by frequent interruption in breathing (apnoea) due to the narrowing or closure of the soft pharyngeal tissue while asleep (3, 4). These repetitive episodes of apnoea cause the patient to wake in response to the deprivation of oxygen and have a significant impact on patient's quality of life. Symptoms can be divided by their time of occurrence into night and day symptoms. Night symptoms include snoring, forced breathing, frequent awakenings, nocturia, gasping and dry mouth (4, 5). Day symptoms include decreased energy and concentration, excessive daytime sleepiness (EDS), memory impairment, irritability, and depression (5). Risk factors for OSA include older age, male gender, obesity and craniofacial and upper airway abnormalities (6).
OSA is a risk factor for several cardiovascular, neurologic and metabolic conditions such as hypertension, diabetes mellitus type 2, coronary artery disease, congestive heart failure, stroke and arrythmias (4). Furthermore, OSA-related EDS has shown to be associated with increased risks of motor vehicle collisions (MVCs) and other accidents (3).

Severity of OSA

The Apnoea Hypopnea Index (AHI) and reductions in blood oxygen levels (oxygen desaturation) are used to classify OSA severity. The AHI is defined as the number of apnoea or hypopneas occurring during an hour of sleep and can be expressed as the number of events per hour (6). Thus, the severity of OSA is classified as follows:

i. None/Minimal: AHI < 5 per hour
ii. Mild: AHI ≥ 5, but < 15 per hour
iii. Moderate: AHI ≥ 15, but < 30 per hour
iv. Severe: AHI ≥ 30 per hour

Oxygen desaturation can be recorded during a study called polysomnography where the patient's breathing pattern is recorded during his/her sleep (6). A normal oxygen saturation at sea level is usually 96-97%. The severity of oxygen desaturation can be classified as follows:

i. Mild: ≥90%
ii. Moderate: 80-89%
iii. Severe: < 80%

Description of treatment strategies

Several therapies are available in the treatment of OSA in routine clinical practice. For patients with mild-to-moderate disease, OSA treatments include positional therapy, dental appliances, and continuous positive airway pressure (CPAP). CPAP is a device that delivers a continuous supply of pressurised air through a mask and is the standard care treatment for patients with moderate-to-severe OSA (4). Intolerance to CPAP therapy is common due to mask discomfort, dry mouth and nasal congestions. This results in a reduced treatment effectiveness with therapy adherence ranging from 50 to 90% in European countries (3). Bilevel positive airway pressures (BiPAP) can be used to treat OSA in morbidly obese patients or in the presence of comorbidities (7).

Surgical intervention can be considered in selected cases of severe OSA with nasal blockage. Hypoglossal nerve stimulation (HNS) might be a more viable treatment for patients who are ineligible for CPAP or dental appliances (3). HNS is delivered via an implantable device that stimulates key airway muscles during sleep via the hypoglossal nerve, allowing the patient's airway to remain open and is indicated in patients with moderate-to-severe OSA, not eligible for CPAP, not significantly obese (body mass index ≤32) and without complete concentric collapse of the upper airway at the soft palate level (4, 8).

How does HNS work

The objective of hypoglossal nerve stimulation is to treat obstructive sleep apnoea by preventing the tongue from prolapsing backwards, causing upper airway obstruction during sleep. It consists of a sensor that registers when the patient stops breathing to send an electrical current that stimulates the hypoglossal nerve. This leads to a contraction of the genioglossus muscle, which is responsible for tongue protrusion (9).

The surgical procedure involves the implant being placed in an infraclavicular subcutaneous pocket under general anaesthetic and then a stimulating lead is placed on the hypoglossal nerve (9).

Three implants have been developed for HNS for patients with moderate or severe OSA who have failed (Apnoea-hypopnoea index (AHI) range from 15-65 with <25% central apnoeas], significantly obese (body mass index 32) and are free of complete concentric

collapse of the upper airway at the soft palate level [16]) CPAP; Inspire®, Aura 6000™ and Nyxoah Genio™.

The underlying principle for the implant systems is the same, but there is some variation in terms of function and design. The implants Inspire and Aura 6000 consist of a wire connected to the hypoglossal nerve on one side of the head, in turn connected to a battery pack in the chest Both implants are activated by means of a remote control. The Nycoah Genio implant is placed under the chin, directly on to both hypoglossal nerves. It does not have an implanted battery pack, but a rechargeable battery is placed on the skin under the chin every night using a band aid. All three implants systems require surgery. Where the patient normally will be able to go home the same day. The Inspire and Aura 6000 systems are similar to a pacemaker in that they involve an implanted battery pack. The packs are expected to last 7 and 5 years, respectively.

Aims

In this rapid HTA we want to map current evidence base regarding the effectiveness, safety and cost associated with the use of hypoglossal nerve stimulation in the treatment of obstructive sleep apnoea. The report is based on a report published by EUnetHTA in 2020 (10).

Methods

The effectiveness and safety results presented in this rapid HTA is a dissemination of findings presented in a health technology assessment published by EUnetHTA in June 2020 (10). We have not performed separate searches from literature, but we have gone through studies listed as ongoing in the EUnetHTA-report in and aim to identify recently published important studies. No protocol was developed for this rapid HTA.

Selection criteria used in EUnetHTA-report

Our rapid HTA disseminates findings in a EUnetHTA-report using the following PICO:

Population	Quote: «Adult patients with moderate-to-severe Obstructive Sleep Apnea (OSA) who presented inadequate adherence* or failure to positive airway pres-sure (PAP) systems or to other non-invasive procedures. »
Intervention	Hypoglossal nerve stimulation
Comparison	No treatment
Outcomes	Apnea-Hypopnea Index (AHI) Oxygen Desaturation Index (ODI) Percentage of sleep time with the oxygen saturation level below 90% Epworth Sleepiness Scale (ESS) Quality of life Technical and Procedural Success Rate of cardiovascular events Rate of cerebrovascular events Overall mortality Adherence to treatment Procedure-related complications Device-related adverse events Other serious adverse events
Studiedesign	Quote: «Effectiveness: Randomized clinical trials (RCTs), prospective non-randomized controlled studies, and other observational comparative studies. Safety: Randomized clinical trials, prospective non-randomized controlled stud-ies, other observational comparative and non-comparative studies, and single-arm studies with > 10 patients. »

Searches for literature

We did not perform separate searches for literature in this rapid HTA. We did, however, go through studies listed as ongoing studies in the EUnetHTA-report (10) to see if any of these studies were published after June 2020. This search was done by using the study ID (NCT number) searching clinicaltrials.gov and pubmed.gov. No additional studies were identified in this process.

Study selection and analyses

We refer to the EUnetHTA report for details about the selection process, risk of bias assessments and analyses (10). The authors of the EUnetHTA report used GRADE to assess the certainty of evidence. Certainty of evidence is in essence a continuous measure, but the GRADE system differs between four main categories as defined in the following:

High certainty	⊕⊕⊕⊕	We are very certain that the effect estimate is close to the true effect size
Moderate certainty	⊕⊕⊕◯	We are moderately certain about the effect: the effect estimate is probably close to the true effect size, but may be different
Low certainty	⊕⊕◯◯	Our certainty in the effect estimate is limited: the true effect size may be significantly different from the estimate
Very low certainty	⊕◯◯◯	Our confidence in the effect estimate is very low

Costs and budget impact analyses

We contacted topic experts to receive information about patient eligibility and expected number of eligible patients. Net and gross prices for the HNS system as well as capital costs (physician programmer) in NOK were provided by Inspire©, anticipating that the costs are similar across different HNS systems.

Results

Effect and safety

Results are based on an HTA published by EUnetHTA in 2020 (10). We did not perform separate systematic searches, but we went through studies listed as ongoing in the EUnetHTA-report aiming to identify recently published important studies. No additional studies were identified.

EUnetHTA only included one comparative study. The included study suggests that patients with OSA who don't respond to CPAP-treatment may benefit from HNS, our confidence in the evidence is very low. Hence, additional research is needed before conclusions can be drawn with respect to positive and negative effects of HNS treatment (ref.EUnetHTA).

The results of the systematic review conducted by EUnetHTA showed that HNS is possibly associated with a reduction in the apnoea-hypopnoea index, reduced desaturation and less hypoxemia during sleep, and increased sleep quality. Moreover, HNS is possibly associated with procedure-related adverse events that require re-operation. Table 1 summarises the absolute effect of HNS compared to no treatment in patients who did not respond to CPAP treatment. A summary of the EUnetHTA report in Norwegian is provided in appendix 1.

Table 1: *Hypoglossal nerve stimulation (HNS) compared to no treatment for patients with obstructive sleep apnoea who do not respond to ventilator (CPAP) treatment.*

Outcomes	**Number of patients**		Absolute effect (95% confidence interval)	Confidence in the results
	HNS n = 23	**No HNS n = 23**	Difference	
Apnoea-Hypopnea-Index (One-week treatment)	1,7	18,2	**16,4** (9,2 to 23,7) *	⨁◯◯◯ Very low
Desaturation index (One-week treatment)	1,6	17,0	**15,4** (8,7 to 22,1) *	⨁◯◯◯ Very low
Hypoxemia % sleep time with d O_2-saturating < 90% (One-week treatment)	-1,0	-6,5	**5,4** (0,1 to 10,7) *	⨁◯◯◯ Very low
Epworth Sleepiness scale (One-week treatment)	-0,3	3,8	**4,2** (2,0 to 6,4) *	⨁◯◯◯ Very low
Serious adverse events First year following treatment	**24 of 868** patients experienced serious adverse events, including the need for reoperation.			⨁◯◯◯ Very low
Serious adverse events, long term follow-up (12 months)	**11 of 868** patients reoperated due to device malfunction			⨁◯◯◯ Very low

[1] Our confidence in the results reflect how sure we can be that results reflect the real-life scenario.
* The figure in parenthesis shows the margin of error, (95 % confidence interval) – a measure of how uncertain the results are due to chance.

Patient base and eligibility

According to expert's opinion, approximately 15 000 patients suffering from OSA initiate CPAP treatment in Norway each year. From these, 20% will not tolerate CPAP, meaning 3000 patients nationally per year who will need other treatment. Half of these patients will receive optional treatment with oral appliances (mandibular advancement device), weight reduction or positional therapy, leaving about 1500 patients nationally who are potential candidates for other treatment.

In Norway, it is assumed that approximately 100 patients would be eligible for treatment with HNS devices per year. This estimate is based on a Finnish study (11) which suggests that patients should be carefully selected for HNS treatment as not all of them can benefit from this approach. Based on experts' estimates, the growth rate of HNS uptake is expected to be between 25% and 30% per year in fully developed market (12). Moreover, experts estimated the lower and upper bounds of the expected number of candidates for HNS per year in a 6- to 8-year time span (13, 14). These estimates

showed that approximately 154 to 264 patients are expected to receive HNS per year in a fully developed market which aligns with our lower and upper bounds of 100 and 286 patients, respectively. We explored three different scenarios with different uptake rates of 25%, 28% and 30% in a 5-year perspective starting with 100 patients in year 1 (Tables 2-4).

T*able 2:* *Number of patients treated with HNS per year at a 25% uptake rate*

Year	1	2	3	4	5
Nr. patients	100	125	156	195	244

Table 3: *Number of patients treated with HNS per year at a 28% uptake rate*

Year	1	2	3	4	5
Nr. patients	100	128	164	210	268

Table 4: *Number of patients treated with HNS per year at a 30% uptake rate*

Year	1	2	3	4	5
Nr.patients	100	130	169	220	286

Costs

System- related costs

Net and gross prices for the HNS system as well as capital costs (physician programmer) in NOK were provided by Inspire© (Table 5). We believed it was reasonable to assume that these costs were similar across different HNS systems (i.e. Nyxhoa Genio®) after discussing with the different providers. Important to highlight is the fact that the Nyxhoa Genio® system does not require a battery nor a remote or a physician programmer, and consequently, costs related to these need to be excluded from calculations. However, once these costs are excluded the total cost for the Nyxhoa Genio® system would be approximately NOK 261,250 which does not differ largely from Inspire© total cost. The system costs include an implantable pulse generator (IPG), stimulation and sensor wire, and the system's remote control. The provider assumed capital costs related to one physician programmer to program the and check the battery and device status annually. In the case of the Inspire© system, the cost of the sleep remote replacement is added to the calculations.

Table 5: *Unit and total costs for a Hypoglossal Nerve Stimulation system*

Description	Quantity	Net price	Gross price
Inspire© IV UAS System*			
Implantable pulse generator (IPG) with non-rechargeable battery for unilateral stimulation of the hypoglossal nerve	1	167,000	208,750
Implantable stimulation wire for the stimulation of the hypoglossal nerve	1	18,000	22,500
Implantable sensor wire to detect respiratory impulses for stimulation of the hypoglossal nerve	1	18,000	22,500
Patient remote control for activation and inactivation of the hypoglossal nerve stimulation system	1	7,000	8,750
Price per system		210,000	262,500
Accessories			
Physician Programmer	1	5,000	6,250
Sleep remote (replacement unit)**	1	3,000	3,750
Total cost for HNS system (price per system+ annual physician programmer)			**268,750**

Note: All costs are in NOK. * These costs are reported for the Inspire© system, however, we consider these costs to be fairly similar to those of Nyxhoa Genio® system after discussions with the provider. **The cost for sleep remote would only be included in case the patient receives the Inspire© system since Nyxhoa Genio ® does not require a remote control.

Patient costs

Based on projections of the yearly uptake of HNS, costs were calculated according to the number of patients per year in each of the three scenarios mentioned in the previous section (i.e. 25%, 28% and 30% uptake rate). The total cost for HNS system was multiplied by the number of patients per year who are potential candidates for HNS therapy. It was assumed that the incidence of patients who are candidates for HNS will increase each year according to the uptake rate. Thus, there will be a "new" cohort of patients receiving HNS each year. The costs in the different scenarios are presented in tables 6-8.

Table 6: *Total costs for HNS treatment at a 25% yearly increase in the use.*

Year	1	2	3	4	5
Nr.patients	100	125	156	195	244
Total cost	26,875,000	33,593,750	41,992,188	52,490,234	65,612,793

Table 7: *Total costs for HNS treatment at a 28% yearly increase in the use.*

Year	1	2	3	4	5
Nr. patients	100	128	164	210	268
Total cost	26,875,000	34,400,000	44,032,000	56,360,960	72,142,029

Table 8: *Total costs for HNS treatment at a 30%yealy increase in the use.*

Year	1	2	3	4	5
Nr. patients	100	130	169	220	286
Total cost	26,875,000	34,937,500	45,418,750	59,044,375	76,757,688

The costs presented above don't include costs related to surgical procedures. The implantation of the device requires open neck surgery in general anesthesia, usually as outpatient procedure. Normal surgical equipment is required, including nerve-stimulator to secure implantation on the correct nerve. There is no specific NCSP-code for this procedure.

Discussion

As this is a cost analysis, and not a complete health technology assessment, we have not conducted a review of economic evaluations in the field. However, the time horizon of our CA is likely to be too short to capture any long-term financial benefits or offsets brought about by HNS. We have therefore provided a brief summary of an economic evaluation from the UK sponsored by one of the manufacturers to illustrate this point. The study by Blissett is not directly transferable to the Norwegian setting, but presents a cost-utility analysis of HNS for OSA from an NHS perspective in the UK (4). The study was commissioned by Inspire Medical Systems. According to the model's base case analysis, patients undergoing HNS will incur lifetime costs of GBP 65 026 and gain 12.72 quality adjusted life years (QALYs) compared to a cost of GBP 36 727 and gains of 11.15 QALYs amongst untreated patients. The incremental cost-effectiveness ratio (ICER) is thus GBP 17 989 per QALY gained for patients with severe OSA who have tried and failed CPAP. One of the assumptions on which the model is based was that patients in the intervention group who experienced successful treatment with HNS improved their overall survival by 14% over a 14-year period. Further, health care utilisation costs are assumed to be higher (19%) in the comparator group due to the higher risk of ischemic heart disease. The ICER rises to approximately GBP 39 000 when the positive effects of HNS on cardiovascular disease and road traffic accidents are removed. The utility values in the study were drawn from a US study of patients before and after CPAP, as there were no direct values available for HNS patients.

The study shows that there may be long term economic and financial benefits associated with HNS. This should be borne in mind when considering the budget impact for all three implants. Moreover, a potential limitation of this analysis was the difficulty surrounding the estimation of the short-term costs to the health care services for patients who are CPAP intolerant and may still require follow-up for OSA-related symptoms or conditions. This did not allow for a direct comparison of costs between patients who do and do not receive HNS therapy. Furthermore, the 5-year time horizon in this analysis is not long enough to capture potential cost savings with HNS implementation, and it is only limited to equipment and capital costs which might impact future reimbursement decisions within the health care system.

Overall, costs for HNS therapy are expected to be higher than those for current treatment and follow up of patients who did not tolerate CPAP. However, these high costs may be offset in the long run given that HNS has proved to have positive effects on cardiovascular disease and road traffic accidents by decreasing their risk and incidence, respectively (4). As this is just a cost analysis, we consider that other type of analyses with a longer time horizon could be performed in the Norwegian setting in order to have a broader overview of cost offsets far in the future.

Conclusion

The effectiveness of hypoglossal nerve stimulation in the treatment of severe obstructive sleep apnoea is very uncertain due to lack of comparative studies. More studies are expected to be published in 2022 and 2023 and will hopefully contribute to more certain conclusions regarding effect and safety. The cost of the HNS system is estimated to NOK 268 750 per patient.

The number patients eligible for treatment with HNS is estimated to 100 in year one with an expected yearly uptake rate between 25 and 30 percent. This corresponds to a yearly total cost about 27 MNOK in year one and 72 MNOK in year five, but these estimates do not take costs related to the surgical procedure into account.

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Appendix 1: Norwegian summary

Virker hypoglossal nervestimulering mot obstruktivt søvnapné?

Utvalgt pasienter med obstruktive søvnapné kan ha nytte av behandling med hypoglossal nervestimulering, men behandlingsmetoden kan også ha bivirkninger. Eksisterende forskningsdata er imidlertid svært usikre, og det trengs mer forskning før vi kan trekke sikre konklusjoner om positive og negative effekter. Det viser en EUnetHTA-oversikt.

Hva sier forskningen?

I systematiske oversikter samles og vurderes tilgjengelig forskning. I denne systematiske EUnetHTA-oversikten var spørsmålet: «Virker hypoglossal nervestimulering bedre enn ingen behandling for pasienter med obstruktivt søvnapné som ikke responderer på behandling med ventilator (CPAP)».

Resultatene viser at hypoglossal nervestimulering:

- kanskje er assosiert med en reduksjon av apné-hypopné-indeks, men disse resultatene er svært usikre
- kanskje er assosiert med redusert desaturering og mindre hypoksemi under søvn, men disse resultatene er svært usikre
- kanskje er assosiert med bedre søvnkvalitet, men disse resultatene er svært usikre
- kanskje er assosierte med utstyr- eller prosedyrerelaterte uønskede hendelser som utløser behov for re-operasjon.

Basert på det tilgjengelige datagrunnlaget er fordelene og ulempene med hypoglossal nervestimulering usikre, ytterligere forskning er nødvendig for å evaluere effekten.

Resultattabell 1: Hypoglossal nervestimulering (HGNS) sammenlignet med ingen behandling for pasienter med obstruktivt søvnapné som ikke responderer på behandling med ventilator (CPAP)

Hva skjer?	Antall pasienter		Absolutt effekt (95% konfidensintervall)	Tillit til resultatet[1]
	HGNS n = 23	Ingen HGNS n = 23	Forskjell	
Apné-Hypopné-Indeks (1 ukes behandling)	1,7	18,2	16,4 (9,2 til 23,7) *	⨁◯◯◯ Svært liten
Desatureringsindeks (1 ukes behandling)	1,6	17,0	15,4 (8,7 til 22,1) *	⨁◯◯◯ Svært liten
Hypoksemi % søvntid med O_2-metning < 90% (1 ukes behandling)	-1,0	-6,5	5,4 (0,1 til 10,7) *	⨁◯◯◯ Svært liten
Epworth søvnighetsskala (1 ukes behandling)	-0,3	3,8	4,2 (2,0 til 6,4) *	⨁◯◯◯ Svært liten
Alvorlige bivirkninger Første år etter behandling	24 av 868 pasienter opplevde alvorlige bivirkninger, herunder behov for reoperasjon.			⨁◯◯◯ Svært liten
Alvorlige bivirkninger Langtidsoppfølging (>12 måneder)	11 av 868 pasienter måtte reopereres da utstyret ikke fungerte			⨁◯◯◯ Svært liten

[1]Tilliten til resultatet handler om hvor trygge vi kan være på at resultatet gjenspeiler virkeligheten.
* Tallene i parentes viser feilmarginen (95 % konfidensintervall) - et mål på hvor usikkert resultatet er på grunn av tilfeldigheter.

Bakgrunn

Obstruktiv søvnapnè er en søvnforstyrrelse som innebærer at pasienten gjentatte ganger stopper å puste under søvn. Fedme kan påvirke de øvre luftveien mekanisk og dermed gi økr risiko for obstruktiv søvnapé. Tilstanden diagnostiseres under polysomnografi i søvnlaboratorium Alvorlighetsgraden kategoriseres etter hvor mange episoder pasienten i gjennomsnitt opplever hver time: 15-30 episoder karakteriseres som moderat søvnapné mens mer enn 30 episoder karakteriseres som alvorlig søvnapné. Ubehandlet obstruktiv søvnapné gir redusert søvnkvalitet, og er assosiert med høyt blodtrykk, kognitive svekkelserog kardiovaskulær sykdom

Pasienter med obstruktiv søvnapné behandles vanligvis med CPAP (Continuous Positive Airway Pressure). Noen pasienter har imidlertid dårlig etterlevelse med eller opplever bivirkninger knyttet til bruk av CPAP, og for disse pasientene kan det være aktuelt å tilby hypoglossal nervestimulering. Behandlingen består i at pasienten får implantert en sensor som registrerer når pasienten slutter å puste og en elektrode som stimulerer musklene i tungen og øvre luftveier når pasienten slutter å puste. På den måten holdes luftveiene åpne under søvn.

Ifølge oversikten fra EUnetHTA er det tre produkter for hypoglossal nervestimulering på markedet i Europa: Inspire®, Aura6000® og Genio®.

Hva er denne informasjonen basert på?

Forfatterne av EUnetHTA-oversikten gjorde et litteratursøk i aktuelle forskningsdatabaser frem til januar 2020. De fant en randomisert kontrollert studie (RCT) som inkluderte 46 personer og sju ikke-kontrollerte studier som inkluderte 868 personer. RCTen inkluderte pasienter som allerede hadde tatt i bruk Inspire®, men for halvparten av pasientene ble systemet skrudd av i observasjonsperioden (1 uke). Pasientene som var inkludert i de ukontrollerte studiene hadde fått implantert ulike systemer for hypoglossal nervestimulering.

Forfatterne av EUnetHTA-oversikten identifiserte 7 pågående studier, 3 av dem er RCTer.

PICO	Hva lette de etter?	Hva fant de?
Populasjon	Hvem er disse personene?	Pasienter med moderat til alvorlig obstruktiv søvnapné som har lav tolerense for eller utilfredsstillende effekt av behandling med CPAP
Tiltak og sammenligning	Hypoglossal nervestimulering sammenlignet med ingen behandling	De fant tre CE-merkede teknologier med godkjent indikasjon: – Inspire®, produsert av InspireMedical Systems – Aura6000® produsert av ImThera Medical – Genio®, produsert av Nyxnoah
Utfall	Apné-hypopné-indeks (AHI), desatureringsindeks, tid med hypoksemi, søvnkvalitet, livskvalitet og uønskede hendelser	RCTen rapporterte på kliniske utfall, men ikke på uønskede hendelser. Søvnkvalitet ble målt med Epworth søvnighetsskala som går fra 0 (ingen problemer) til 24 (stort problem).
Setting	Hvilke land?	RCTen er en multisenter studie fra USA og Europa
Tillit til resultatet	Overiktsforfatterne brukte GRADE for å vurdere tilliten til dokumentasjonsgrunnlaget for hvert utfall.	Tilliten til dokumentasjonsgrunlaget for utfallene var gjennomgående svært lav på grunn av risiko for bias og upresise data (få studier/få deltakere).

*Common Terminology Criteria for Adverse Events (CTCAE) er et sett med kriterier for standardisert klassifisering av bivirkninger av legemidler som brukes i kreftterapi.
**Expanded Prostate Cancer Index Composite (EPIC) er spørreskjema utviklet for å overvåke helserelaterte livskvalitetsutfall blant menn behandlet for prostatakreft

Systematisk oversikt

I systematiske oversikter søker man etter og oppsummerer studier som svarer på et konkret forskningsspørsmål. Studiene blir funnet, vurdert og oppsummert ved å bruke en systematisk og forhåndbeskrevet fremgangsmåte

Tillit til resultatet (GRADE)

Når vi oppsummerer studier og presenterer et resultat, så er det viktig å si noe om hvor mye tillit vi kan ha til dette. Det handler om hvor trygge vi kan være på at resultatet gjenspeiler virkeligheten. GRADE er et system vi bruker for å kunne bedømme tilliten til resultatet. I GRADE vurderer vi blant annet:

- hvor godt studiene er gjennomført
- om studiene er store nok
- om studiene er like nok
- hvor relevante studiene er
- om alle relevante studier er fanget opp

Kilde

EUnetHTA OTCA21 Authoring Team. Hypoglossal nerve stimulation systems for treatment of obstructive sleep apnea. Collaborative Assessment. Diemen (The Netherlands): EUnetHTA; 2020. Report No.: OTCA21. Available from https://www.eunethta.eu

Appendix 2: Activity log

NIPH submits «Metodevarsel»	14.10.2020
Commissioning forum commissioned a rapid HTA	14.12.2020
Content experts appointed	05.05.2021
Draft shared with experts	12.01.2022
Draft accepted by experts	21.01.2022
Rapid HTA approved at NIPH	23.01.2022
Rapid HTA submitted to New methods	24.01.2022

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